REMARKS

I. Claim Status.

Claims 2-11 and 13-28 are pending in the application. Claim 1 and 12 are cancelled and Claims 2-6, 8-11 and 22-28 are withdrawn from consideration. This Response and Amendment amends Claim 7 and adds new Claims 29-36.

II. Claim Amendments

Claim 7 is amended to clarify that the reagent mixture is "suitable for use in flow cytometry." Support for the amendment can be found throughout the specification, e.g., on page 10 line 4 and page 13 lines 16-17.

Support for new Claim 29 can be found in original Claim 2.

Support for new Claim 30 can be found in original Claim 3

Support for new Claim 31 can be found in original Claim 1

Support for new Claim 32 can be found in original Claim 1.

Support for new Claim 33 can be found on page 8 lines 9-13 of the specification.

Support for new Claim 34 can be found in original Claim 1.

Support for new Claim 35 can be found, e.g., on page 10, lines 11-14 and on page 30 lines 18-22 of the specification.

Support for new Claim 36 can be found on page 10, lines 9-11.

Applicants respectfully submit the amended and new claims do not contain new matter and are believed to fall within the Group and Species elected in response to the restriction/election requirements set forth below.

III. Restriction/Election Requirement.

In the papers dated 4/27/05 and 4/22/05, Applicants elected Group I, claims 2-12 and 22-23, with traverse. Further, Applicants elected species D, with traverse, antigen- or antibody sensors.

Applicants' invention is directed to a reagent mixture of different classes of sensor

particles, and requires particles from classes (a), (b) and at least one of (c), (d) or (e). The Office has restricted Applicants invention to only one of classes (c), (d), and (e). However, the Examiner has agreed to consider the non-elected species of Claim 9, 11 and 22, i.e., (c) enzyme-sensor particles and (e) nucleotide sequence-sensor particles, as additional species should the elected species be found allowable. Claims 1-5 are dependent on Claim 22. Accordingly, Applicants respectfully request reconsideration of Claims 1-5 should the elected species be found allowable.

IV. The Rejection Under 35 USC § 103.

The Office has rejected Claim 7 under 35 USC § 103(a) as being unpatentable over McDevitt et al (US 6,680,206) in view of Van den Engh et al (US 5,747,349) for the reasons stated in numbered paragraphs 6 and 7 of the Office Action. Applicants respectfully traverse these rejections because the Office has not provided the requisite motivation to combine the references, nor any reasonable expectation of success for the combination. Indeed the references, taken as whole, teach away from the claimed combination.

McDevitt et al (US 6,680,206)

McDevitt et al. does not disclose "a reagent mixture of different classes of sensor particles in a fluid suitable for use in flow cytometry" as required by independent Claim 7. However, the Office states that McDevitt et al. discloses "sensor arrays comprising plurality of sensitive particles (sensor particles) for identification of multiple analytes in a sample . . . ." (Office Action, page 7, par. 12). The Office has not asserted that McDevitt discloses a reagent mixture of different classes of particles, and in fact, McDevitt does not disclose such a mixture of particles.

The McDevitt et al. reference as a whole, is primarily directed to a system, including, a light source, a sensor array and a detector, as well as various designs for supporting members, which segregate chemically sensitive particles into an ordered array. (Col. 4, line 26-28; col. 8, lines 2-3, 17-19, and 41-47). The particles are placed in predefined locations on the array by micromanipulators to create an ordered array having a predefined configuration of particles, or the particles may be randomly placed within the cavities and calibrated to determine the identity of the particle at any specified location on the array (Col. 10, lines 9-17).

Among the multitude of chemically sensitive particles mentioned for inclusion in the system are particles containing receptors for DNA, RNA, proteins, enzymes, oligonucleotides, antigens, polythioureas, polyguanidiniums and imprinted polymers. However, McDevitt provides working examples for only two classes of particles, in accordance with applicants claimed invention, namely three dye based sensors for electrolytes and one boronic acid sugar receptor. Thus any suggestion within McDevitt et al. to include particles containing receptors for DNA, RNA, proteins, enzymes, oligonucleotides, antigens, polythioureas, polyguanidiniums and imprinted polymers falls squarely within the admonition that "obvious to try" is not the standard under § 103. This admonition has been directed mainly at two kinds of error.

> In some cases, what would have been 'obvious to try' would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful.... In others, what was 'obvious to try' was to explore a new technology or general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it." *In re O'Farrell*, 853 F.2d 894, 903, 7 USPQ2d 1673, 1681 (Fed. Cir. 1988)

More particularly, McDevitt's inclusion of antibodies and antigens as alternatives appear despite the reference's earlier teaching that:

> Most antibody methods are relatively insensitive and require the presence of 10^5 to 10^7 organisms. The response time of antibody-antigen reactions in diagnostic tests of this type ranges from 10 to 120 minutes, depending on the method of detection. The fastest methods are generally agglutination reactions, but these methods are less sensitive due to difficulties in visual interpretation of the reactions. Approaches with slower reaction times include antigen recognition by antibody conjugated to either an enzyme or chromophore. These test types tend to be more sensitive, especially when spectrophotometric methods are used to determine if an antigen-antibody reaction has occurred. These detection schemes do not, however, appear to allow the simultaneous detection of multiple analytes on a single detector platform. (McDevitt et al., col. 3, lines 42-56)

Thus, McDevitt et al. clearly criticizes, discredits and otherwise discourages the inclusion of antibody or antigen sensors in multi-analyte applications due to problems with sensitivity, speed and/or versatility.

Moreover Applicants' claimed particle mixture, and inherent, common reaction

environment, is subject to more restrictive assay constraints than in the micromachined array described in McDevitt. All of the particles in Applicants' claimed mixture are subjected to a common reaction milieu, and the common reaction environment allows for reactions between particles that have diffusible reaction products. The common reaction environment means that assays on some particles are suboptimized in order to allow effective assay on other particles. As described in the specification, Applicants designed an effective assay for multiple particles in suspension, which balances the competing needs of different assays.

In contrast, McDevitt teaches the desirability of isolating each particle into an individual reactor cell where its assay conditions are locally altered to better suit the individual assays. For example, McDevitt teaches (cols. 41 and 42) that a fluid may be selectively pumped into a designated reactor cell to alter conditions (as by releasing a reagent bound to a particle) in that cell, but not in all cells.

Accordingly, the McDevitt et al. reference fails to provide the requisite motivation to combine ion, metabolite and antigen or antibody sensor particles as a mixture in a fluid. Moreover, the McDevitt et al. reference is devoid any teaching providing a reasonable expectation of success that modifying such a combination would be suitable for use in flow cytometry.

Van den Engh et al (US 5,747,349)

The Van der Engh et al. reference fails to cure the deficiencies of the McDevitt et al. reference. Van den Engh et al. does not disclose a reagent mixture of different classes of sensor particles, the reagent mixture comprising sensor particles selected from each of the classes (a), ion-sensor particles; class (b), metabolite-sensor particles, and class (d) antigen- or antibody-sensor particles.

Van den Engh summarizes the analytes which can be measured with the reporter beads of the invention, stating:

> Analytes which can be measured using reporter beads of this invention include pH, O_2, CO_2, Ca^{+2}, Na^+, K^+, Cl^-, other halides, Mg^{+2}, Zn^{+2}, Tb^{+3}, and other metal ions including alkali and alkaline-earth ions, ionic strength, solvent polarity, albumin, alcohols, pesticides, organic salts such as lactate, sugars such as glucose, heavy metals, and drugs such as salicylic acid, halothane and narcotics.

(Van den Engh, Col. 3, lines 5-12).

No where in this exhaustive laundry list of analytes, are antibodies or antigens listed.

Further, there is no motivation to modify or combine Van der Engh with McDevitt, as Van de Engh specifically teaches away from Applicants claimed invention. Van der Engh teaches in the Background section that "antigens in the fluid can be detected by the aggregation of antibody coated fluorescent beads." (Van der Engh, col. 1, lines 62-64). However, the reference then teaches the following in the Detailed Description of the Invention:

> In contrast with the previously used reporter beads, wherein the number of beads in an aggregate changes, in the present invention the fluorescence of each individual bead changes. In further contrast, the reporter beads of this invention ***are not required to have*** an immunoreagent, such as a ligand, antiligand, ***antigen or antibody***, on the surface in combination with the reporter molecules." (Col. 3, lines 60-64, emphasis added).

Further,

> The interaction ***need not be a ligand/antiligand or antigen/antibody reaction***. The interaction preferably does not lead to an aggregate with other particles and, in particular, does not create an aggregate containing a plurality of reporter beads. (Col. 4, lines 13-18).

When the Van der Engh reference is taken as whole, it is apparent that combining antigen- or antibody sensor particles with the other particles described in Van den Engh, is not contemplated or desirable. Moreover, the reference fails to provide the requisite motivation to combine the antigen or antibody receptors listed in McDevitt et al. with other types of reporter beads listed in Van der Engh. Likewise, Van der Engh et al provide no reasonable expectation of success for using such a mixture of particles in multi-analyte flow cytometry applications due to the well known attribute of antibodies and antigens to form aggregates.

CONCLUSION

Neither the McDevitt et al. nor the Van der Engh et al. reference teach or suggest a mixture of sensor particles suitable for flow cytometry, which includes ion-, metabolite- and antigen/antibody sensors. In contrast, both references teach the shortcomings of antigen/antibody sensors in multi-analyte assays. Accordingly, the claimed combination is not obvious and Applicants request withdrawal of the rejection under 35 U.S.C. § 103 as well as allowance of Claim 7.

New claims 29-36 all depend from independent Claim 7 and are likewise considered to be novel and non-obvious on this basis. Applicants further note that both McDevitt et al. and Van der Engh et al. are silent with respect to the "target ionophore" Claim 31, the "analogue" of Claim 33 or 36, and the "reporter antibody" of Claim 36. Thus, McDevitt et al. and Van der Engh et al. do not teach all the elements of these dependent claims.

The Applicant believes that all pending claims are in condition for allowance and such action is earnestly requested. If the present amendments and remarks do not place the Application in condition for allowance, the Examiner is encouraged to contact the undersigned directly if there are any issues that can be resolved by telephone with the Applicants representative.

The Commissioner is authorized to charge $450.00, the fee for a two-month extension, to deposit account No. 19-2090. No other fees are believed due with this Response. However, if any fees are due, the Commissioner is authorized to charge any such fees to deposit account No. 19-2090.

Respectfully Submitted,
SHELDON MAK ROSE & ANDERSON

Date: March 12, 2007

By /Margaret Churchill/
Margaret Churchill, Ph.D.
Reg. No. 39,944

SHELDON MAK ROSE & ANDERSON, PC
225 South Lake Avenue, 9th Floor
Pasadena, California 91101-3005

Telephone (626) 796-4000
Facsimile (626) 795-6321